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1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,107	HEYDUK ET AL.	
	Examiner	Art Unit	
	NARAYAN K. BHAT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *109-130* is/are pending in the application.

4a) Of the above claim(s) *112-115,117 and 128-130* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *109-111,116 and 118-127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/28/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 109-130 are pending in this application.

Election/Restrictions

2. Examiner has requested to elect a single biosensor having 2 or more epitope binding agents selected from the species: antibody/antibody, antibody/aptamer, antibody/dsNA, aptamer/aptamer, aptamer/dsDNA, dsNA/dsNA, antibody/antibody/antibody, antibody/antibody/aptamer, antibody/antibody/dsNA, antibody/aptamer/dsNA, aptamer/aptamer/aptamer, aptamer/aptamer/antibody, aptamer/aptamer/dsNA, dsNA/dsNA/dsNA, dsNA/dsNA/antibody, and dsNA/dsNA/aptamer, for prosecution on the merits.

3. Applicant's election with traverse of species wherein the biosensor consisting of two epitope binding agents, wherein each epitope binding agent is an antibody for initial prosecution on the merits in the reply filed on April 16, 2007 is acknowledged. The traversal is on the ground(s) that election of species is not proper because the species share a special technical feature. This is not found persuasive because of the following reasons.

The antibodies as an epitope binding agents lack any structural feature in common with the nucleic acids and the aptamers because the antibodies are polypeptides and the aptamers and nucleic acids are not. The nucleic acids and aptamers are judged to lack any significant common structural feature because

although they are both nucleic acids, aptamers are generally single stranded nucleic acids that fold up to assume a particular secondary and tertiary structure that recognizes an epitope, whereas double stranded nucleic acids, in view of the specification as a whole are intended to refer to e.g. sites for DNA-binding proteins, and comprise separate single stranded molecules joined by hybridization of complementary base pairs. The requirement is still deemed proper and is therefore made FINAL.

4. Claims 112-115, 117 and 128-130 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species there being no allowable generic or linking claim. Applicant timely traversed the election of species requirement in the reply filed on April 16, 2007.

5. Claims 109-111, 116 and 118-127 are under prosecution.

6. Examiner has changed for the prosecution of this application. Please send future correspondence to Dr. Narayan K. Bhat, AU 1634.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 109-111, 116, 118-122 and 124-127 are rejected under 35 U.S.C. 102(b) as being anticipated by Baez et al (USPGPUB NO. 2002/0051986 published may 2, 2002) as evidenced by SantaLucia (PNAS, 1998, 95, 1460-1465).

Regarding claim 109, Baez et al teaches a molecular biosensor, the biosensor having two nucleic acid constructs, the nucleic acid constructs comprising a nucleic acid reporter conjugates A and A1, which have the structural features of R1-R2-R3-R4 (Fig. 1, #A) and R5-R6-R7-R8 respectively (Fig. 1, #A1). Baez et al further teaches that the nucleic acid reporter conjugate 'A' includes an epitope binding agent that binds to a first epitope C1 on a target molecule (Fig. 1, Right panel, Analyte # B, first epitope on a target molecule # C1, paragraph 0089) and further teaches epitope binding agent comprise antibody (paragraph 0183, structural feature 'R1'), which is the selected species of the instant claim. Baez et al further teaches that the nucleic acid reporter conjugate 'A1' includes an epitope binding agent that binds to a first epitope C2 on the target molecule (Fig. 1, Right panel, Analyte # B, second epitope on a target molecule # C2, paragraph 0089) and further teaches epitope binding agent comprise antibody (paragraph 0183, structural feature 'R5'), which is the selected species of the instant claim.

Baez et al also teaches that nucleic acid reporter conjugate 'A' and 'A1' (Fig. 1) are formed by attaching oligonucleotides to antibodies via linker SATA and sulfo SMCC, specifically attaching antibody (i.e., first epitope binding agent) to a nucleic acid sequence T66 to produce 'A' and attaching antibody (i.e., second epitope binding agent) to a second nucleic acid sequence T68 to produce 'A1' (paragraphs 0165-0174). Baez

et al further teaches that T66 and T68 comprise seven base pair complementary region at the 3' end (Fig. 3, Second panel from the top, Table 1, paragraphs 0182-0183). The nucleic acid region comprising the complementary region in 'A' and 'A1' are the 'R3' and 'R7' of the instant claim. The linker comprising nucleic acid region not complementary to the nucleic acids in 'A' and 'A1' are the flexible linker R2 (i.e., in nucleic acid reporter conjugate 'A') and R6 (i.e., in nucleic acid reporter conjugate 'A1') of the claim. Teachings of Baez et al thus encompass R2 linker attaching R1 to R3 and R6 linker attaching R5 to R7 (paragraphs 0165-0171 and 0183).

Baez et al also teaches that binding of an analyte to nucleic acid reporter conjugates comprising first and second epitope binding agents brings the complementary sequences of the R3 and R7 into proximity to produce analyte specific amplicons (paragraph 0183). Baez et al also teaches a reaction temperature of 25C (paragraph 0184) and salt concentration of 50 mM to carry out amplification reaction comprising analyte specific amplicons (paragraph 0190), thus teaching temperature and salt concentration within the range from about 21C to about 40C and about 1 mM to about 100 mM as claimed.

Baez et al also teaches that the complementary sequences of R3 and R7 have "GCGGGCT" sequence (Fig. 3, Second panel from the top, Table 1, paragraphs 0182-0183). The "GCGGGCT" nucleotide sequence has a free energy of association of 6.91 kcal/ mole accounting for the salt dependence (6X0.98 (for the G*C) + 1x 1.03 (for the A*T) = 6.91kcal/mole) as taught by SantaLucia et al (Abstract, Table 1, last column). It is noted that the reference of SantaLucia for the calculation free energy is used only to

confirm the known fact in the art of free energy of association of complementary nucleotide sequences. Teachings of Baez et al of the complementary nucleotide sequences having a free energy of 6.91 is within the range of about 5.5 kcal/mole to about 8.0 kcal/mole as claimed (structural feature of 'R3' and 'R7' of the claim).

Baez et al also teaches that the nucleic acid molecule of the reporter conjugate A and A1 contain fluorophore labels (paragraph 0139, Label on 'A' – 'R4', label on 'A1'-'R8'). Baez et al further teaches that they are brought into close proximity to each other by binding of reporter conjugates to an analyte to form analyte dependent reporter complex, resulting in fluorescent energy transfer from one fluorophore to the other causing a shift in the emission spectrum thereby detecting the analyte (paragraphs 0137-0139), thus teaching bringing R4 and R8 together produce a signal only when R3 associates with R7. The fluorescence resonance energy transfer taught by Baez et al (paragraphs 0137-0139) is a detection means of the claim.

Regarding claim 110, Baez et al teaches that the target molecule is selected from the group consisting of an analyte, a protein, a polypeptide, a nucleic acid, a biomolecule, a macromolecular complex and a microbial organism (paragraphs 0050 and 0052).

Regarding claim 111, Baez et al teaches that the target molecule is a protein or polypeptide (paragraph 0052).

Regarding claim 116, Baez et al teaches that the R1 and R5 are each antibodies (paragraph 0183).

Regarding claim 118, Baez et al teaches an embodiment wherein the T66 and T68 nucleic acid sequences comprising 68 and 66 nucleotides attached to the antibody via linker (Table 1, paragraph 0183). Baez et al also teaches that T66 and T68 nucleic acid sequence has seven base sequence complementary to each other (paragraph 0183, i.e., R3 and R7 sequences) thus teaching linker comprising T66 and T68 nucleic acid sequence has 58 and 56 nucleotide sequence non complementary to each other, which are R2 and R6 structure of the claim, which is within the range of about 10 to about 100 nucleotides in length.

Regarding claims 119 and 120, Baez et al teaches that antibodies are covalently coupled to the nucleic acid molecules T66 or T68 via linker (paragraphs 0165-174, 0183, limitation of claim 120) thus teaching R2 forms a bond with each of R1 and R3 and R6 forms a bond with each of R5 and R7 (limitation of claim 119). The free energy of the formed bond is interpreted broadly as an obvious variant of the molecular sensor taught by Baez et al.

Regarding claim 121, Baez et al teaches a Sulfo-SMCC bifunctional chemical crosslinker (paragraphs 0165 and 0169) that is used to couple antibodies to nucleic acid molecules to generate A and A1 nucleic acid reporter conjugates (paragraphs 0165-0174) thus teaching R2 and R6 comprising of SMCC a bifunctional chemical crosslinker.

Regarding claim 122, Baez et al teaches a Sulfo-SMCC bifunctional chemical crosslinker (paragraphs 0165 and 0169). Sulfo-SMCC bifunctional chemical crosslinker has a length of 11.9 angstrom as taught by Uptima brochure (pg. 2, paragraph 4). It is

noted that the reference of Uptima brochure is used only to confirm the known fact in the art of linker length. It is also noted that the claim recitation of R2 and R6 from Zero to 500 angstrom in length, indicates that R2 and R6 are not needed when the length of the bifunctional cross linker is zero angstrom.

Regarding claim 124, Baez et al teaches that the R3 and R7 are seven nucleotide in length (paragraph 0183), which is within the range from about 4 to about 15 nucleotide in length as claimed.

Regarding claims 125 and 126, Baez et al teaches that the nucleic acid molecule of the reporter conjugate 'A' and 'A1' contain fluorophore labels (paragraph 0139, Label on 'A' – 'R4', label on 'A1'-'R8'). Baez et al further teaches that they are brought into close proximity to each other by binding of reporter conjugates to an analyte to form analyte dependent reporter complex, resulting in fluorescent energy transfer from one fluorophore to the other causing a shift in the emission spectrum, i.e., FRET (limitation of claim 126) thereby detecting the analyte (paragraphs 0137-0139), thus teaching bringing R4 and R8 together produce a signal only when R3 associates with R7 (limitation of claim 125).

Regarding claim 127, Baez et al teaches a molecular biosensor, the biosensor having two nucleic acid constructs, the nucleic acid constructs comprising a nucleic acid reporter conjugates 'A' and 'A1', which have the structural features of R1-R2-R3-R4 (Fig. 1, #A) and R5-R6-R7-R8 respectively (Fig. 1, #A1). Baez et al further teaches that the nucleic acid reporter conjugate 'A' includes an epitope binding agent that binds to a first epitope C1 on a target molecule (Fig. 1, Right panel, Analyte # B, first epitope on a

target molecule # C1, paragraph 0089) and further teaches epitope binding agent comprise antibody (paragraph 0183, structural feature 'R1'). Baez et al further teaches that the nucleic acid reporter conjugate 'A1' includes an epitope binding agent that binds to a first epitope C2 on the target molecule (Fig. 1, Right panel, Analyte # B, second epitope on a target molecule # C2, paragraph 0089) and further teaches epitope binding agent comprise antibody (paragraph 0183, structural feature 'R5').

Baez et al also teaches that nucleic acid reporter conjugate 'A' and 'A1' (Fig. 1) are formed by attaching oligonucleotides antibodies via linker SATA and sulfo SMCC, specifically attaching antibody (i.e., first epitope binding agent) to a nucleic acid sequence T66 to produce 'A' and attaching antibody (i.e., second epitope binding agent) to a second nucleic acid sequence T68 to produce 'A1' (paragraphs 0165-0174). Baez et al further teaches that T66 and T68 nucleic acid comprise seven base pair complementary region at the 3' end (Fig. 3, Second panel from the top, Table 1, paragraphs 0182-0183). The nucleic acid region comprising the complementary region in 'A' and 'A1' are the 'R3' and 'R7' of the instant claim.

Baez et al also teaches a Sulfo-SMCC bifunctional chemical crosslinker (paragraphs 0165 and 0169). Sulfo-SMCC bifunctional chemical crosslinker has a length of 11.9 angstrom as taught by Uptima brochure (pg. 2, paragraph 4). It is noted that the reference of Uptima brochure is used only to confirm the known fact in the art of linker length. Baez et al also teaches that T66 and T68 nucleic acid sequence has seven base sequence complementary to each other (Table 1, paragraph 0183, i.e., R3 and R7 sequences) thus teaching linker comprising T66 and T68 nucleic acid sequence

has 58 and 56 nucleotide sequence non complementary to each other, which are R2 and R6 structure of the claim. The nucleic acid portion of the linker has a length of about 200 angstrom (~ 60 nucleotides x 3.4 angstrom (for each nucleotide) = 204 angstroms) and combined length of the linker is about 216 angstrom, which is within the range from 0 to about 500 angstrom in length as claimed. It is also noted that the claim recitation of R2 and R6 from Zero to 500 angstrom in length, indicates that R2 and R6 are not needed when the length of the flexible linker is zero angstrom.

The linker comprising nucleic acid region not complementary to the nucleic acids in 'A' and 'A1' are the flexible linker R2 (i.e., in nucleic acid reporter conjugate 'A') and R6 (i.e., in nucleic acid reporter conjugate 'A1') of the claim. Teachings of Baez et al thus encompass R2 linker attaching R1 to R3 and R6 linker attaching R5 to R7 (paragraphs 0165-0171 and 0183).

Baez et al also teaches that binding of an analyte to nucleic acid reporter conjugates comprising first and second epitope binding agents brings the complementary sequences of the R3 and R7 into proximity to produce analyte specific amplicons (paragraph 0183). Baez et al also teaches a reaction temperature of 25C (paragraph 0184) and salt concentration of 50 mM to carry out amplification reaction comprising analyte specific amplicons (paragraph 0190), thus teaching temperature and salt concentration within the range from about 21C to about 40C and about 1 mM to about 100 mM as claimed.

Baez et al also teaches that the complementary sequences of R3 and R7 have "GCGGGCT" sequence (Fig. 3, Second panel from the top, Table 1, paragraphs 0182-

0183). The "GCGGGCT" nucleotide sequence has a free energy of association of 6.91 kcal/ mole accounting for the salt dependence (6X0.98 (for the G*C) + 1x 1.03 (for the A*T) = 6.91kcal/mole) as taught by SantLucia et al (Abstract, Table 1, last column). It is noted that the reference of SantaLucia for the calculation free energy is used only to confirm the known fact in the art of free energy of association of complementary nucleotide sequences. Teachings of Baez et al of the complementary nucleotide sequences having a free energy of 6.91 is within the range of about 5.5 kcal/mole to about 8.0 kcal/mole as claimed (structural feature of 'R3' and 'R7' of the claim).

Baez et al also teaches that the nucleic acid molecule of the reporter conjugate ' A' and 'A1' contain fluorophore labels (paragraph 0139, Label on 'A' – 'R4', label on 'A1'-'R8'). Baez et al further teaches that they are brought into close proximity to each other by binding of reporter conjugates to an analyte to form analyte dependent reporter complex, resulting in fluorescent energy transfer from one fluorophore to the other causing a shift in the emission spectrum thereby detecting the analyte (paragraphs 0137-0139), thus teaching bringing R4 and R8 together produce a signal only when R3 associates with R7. The fluorescence resonance energy transfer (FRET) taught by Baez et al (paragraphs 0137-0139) is a detection means of the claim.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to

> a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 109 and 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Baez et al (USPGPUB NO. 2002/0051986 published may 2, 2002) as evidenced by SantaLucia (PNAS, 1998, 95, 1460-1465) in view of Zalipsky (Advanced Drug Delivery Reviews, 1995, 16, 157-182).

Claim 123 is dependent from claim 109. The teachings of Baez et al regarding claim 109 are described in section 8 of this office action.

Regarding claim 123, Baez et al teaches nucleic acid reporter conjugate comprising sulfo SMCC heterobifunctional linker with nucleic acids comprising R2 and R6 (paragraph 0169) but is silent about polyethylene glycol. However polyethylene glycol was known at the time of the claimed invention was made as taught by Zalipsky, who teaches polyethylene glycol linker to conjugate a variety of ligands (Fig. 1, Table 1) and further teaches that increases stability and solubility of the polyethylene glycol conjugate (Table 1, see comments section). Zalipsky also teaches polyethylene glycol

has a molecular weight of 1000 daltons and has a general structure of HO-(CH2-CH2O)n –CH2-CH2-OH thus teaching the n value of about 23 (pg. 158, column 2, paragraph 2). Wikipedia brochure teaches that C-C bond length is 1.54 angstrom and C-O bond length is 1.43 angstrom (See the brochure). Polyethylene glycol with 1000 molecular weight has the length of about 70 angstrom unit (C-C bond length 1.54 angstrom + C-O bond length 1.43 angstrom; polyethylene glycol 1000 = 23 (1.54+ 1.43)=~ 70 angstrom unit). It is noted that Wikipedia brochure is used to confirm the known fact about the C-O and C-C bond length. The polyethylene glycol taught by Zalipsky of 70 angstrom length is within the claimed range from zero to 500 angstrom in length. It is also noted that the claim recitation of R2 and R6 from Zero to 500 angstrom in length, indicates that R2 and R6 are not needed when the length of the bifunctional cross linker is zero angstrom.

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the sensor structure of Baez et al and include the polyethylene glycol linker of Zalipsky with a reasonable expectation of success.

An artisan would have been motivated to modify the sensor structure of Baez et al and include the polyethylene glycol linke of Zalipsky with the expected benefit of increasing stability and solubility of the polyethylene glycol conjugate as taught by Zalipsky (Table 1, see comments section).

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 109-111, 116, 118-127 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. 11/836,339 in view of Baez et al (USPGPUB NO. 2002/0051986 published may 2, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Regarding instant claims 109 and 127, the claim 1 of copending '339 application is drawn to a molecular biosensor comprising R47-R48-R49-R50 and R51-R52-R53-R54 and has structural features of epitope binding agent (R47 and R51), flexible linkers (R48 and R52), complementary nucleic acid sequences (R49 and R53) and detection means (R50 and R53). Additional structural limitation of flexible linkers, nucleic acid

composition and detection means of instant claim 127 are taught by claims 2-6 of the copending '339 application. The molecular biosensor of the claim 1 of copending '339 application differs from the instant claim 1 and 127 molecular biosensor in the epitope binding agent structural features, specifically, R47 epitope binding agent is not an antibody molecule (as required by the instant claim 127) and the other epitope binding agent, R51, does not bind to a target molecule (as required by claim 1 and 127).

However, epitope binding agents binding to the first and second epitope on the target molecule were known in the art at the time of the claimed invention was made as taught by Baez et al, who teaches the nucleic acid labeled reporter conjugates selectively binding to the two epitopes on the analyte molecule (Fig. 1, Left panel, nucleic acid reporter conjugates, # A and A1, Analyte # B, Epitope binding agents A and A1 binding C1 and C2 epitopes on the analyte, paragraph 0089) and further teaches that epitope binding agents comprise antibodies (Fig. 1, left panel, Example 1, paragraphs 0122, 0182-0183). Baez et al also teaches that binding of two reporter conjugates to the same analyte molecule provides the necessary spatial alignment to enable nucleic acid labels to be joined enzymatically to form an analyte specific amplicons, which greatly enhances the ability to detect analytes at low concentrations (paragraphs 0088-0089).

It would have been obvious to one having the ordinary skill in the art to include nucleic acid constructs with two epitope binding agent for the same target molecule of Baez et al into the claim 1 of the copending '339 application with the expected benefit of binding of two epitope binding agents to the same analyte molecule providing the

necessary spatial alignment to enable nucleic acid labels to be joined enzymatically to form an analyte specific amplicons, which greatly enhances the ability to detect analytes at low concentrations as taught by Baez et al (paragraphs 0088-0089 and 0183).

It is also noted that Baez et al further discloses additional limitations required by instant dependent claims 110-111, 116 and 118-126 as described in detail in this office action in section 8. Therefore the embodiments of claims 110-111, 116 and 118-126 are also obvious for the same reasons given above for instant claims 109 and 127. Dependent claims 110-111, 116 and 118-126 are obvious over claims 1-11 of the '339 copending application in view of Baez et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 109-111, 116, 118-127 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 11/836,333 in view of Baez et al (USPGPUB NO. 2002/0051986 published may 2, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Regarding instant claims 109 and 127, the claim 1 of copending '333 application is drawn to a molecular biosensor comprising R24-R25-R26-R27 and R28-R29-R30-R31 and has structural features of epitope binding agent (R24 and R28), flexible linkers (R25 and R29), nucleic acid sequences (R26 and R30) and detection means (R27 and R31), wherein epitope binding agents R24 and R28 bind to the first and second

epitopes on the target molecule and further comprises of antibody (claim 5 of the copending '333 application, limitations of instant claim 127). Additional structural limitation of flexible linkers, nucleic acid composition and detection means of instant claim 127 are taught by claims 2, 6-8 of the copending '333 application. Biomolecular sensor of claims 1 and 5-8 of copending '333 application differs from the molecular biosensor of instant claim 109 and 127 in that the R26 and R30 nucleic acids are not complementary to each other.

However, nucleic acid structure complementary to each other were known in the art at the time of the claimed invention was made as taught by Baez et al, who teaches the nucleic acid labeled reporter conjugates selectively binding to the two epitopes on the analyte molecule (Fig. 1, Left panel, nucleic acid reporter conjugates, # A and A1, Analyte # B, Epitope binding agents A and A1 binding C1 and C2 epitopes on the analyte, paragraph 0089) and further teaches that A and A1comprise nucleic acid sequences (similar to R26 and R30) and are complementary (Fig. 3, Second panel from the Top, paragraph 0183). Baez et al also teaches that nucleic acid complementary regions serve as extension primers to produce the double stranded DNA to form an analyte specific amplicons, which greatly enhances the ability to detect analytes at low concentrations (paragraphs 0088-0089 and 0183).

It would have been obvious to one having the ordinary skill in the art to include nucleic acid constructs with complementary regions of Baez et al into the claim 1 of the copending '333 application with the expected benefit of providing double stranded DNA to form an analyte specific amplicons, which greatly enhances the ability to detect

analytes at low concentrations as taught by Baez et al (paragraphs 0088-0089 and 0183).

It is also noted that Baez et al further discloses additional limitations required by instant dependent claims 110-111, 116 and 118-126 as described in detail in this office action in section 8. Therefore the embodiments of claims 110-111, 116 and 118-126 are also obvious for the same reasons given above for instant claims 109 and 127. Dependent claims 110-111, 116 and 118-126 are obvious over claims 1-9 of the '333 copending application in view of Baez et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

15. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on (571)-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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Examiner, Art Unit 1634

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